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THE JOURNAL OF  
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C O N T E N T S

VOLUME 46:1 • SPRING 2018

Symposium Articles

SYMPOSIUM

The Future  
of Informed  
Consent in  
Research &  
Translational  
Medicine:  
A Century of  
Law, Ethics &  
Innovation

Guest edited by  
Susan M. Wolf,  
Ellen Wright  
Clayton and  
Frances Lawrenz

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*Letter from  
the Editor*

Cover image ©Getty Images

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**Introduction**

*Susan M. Wolf, Ellen Wright Clayton  
and Frances Lawrenz*

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**Where Did Informed Consent for  
Research Come From?**

*Alexander Morgan Capron*

To understand the future of informed consent, we should pay attention to two ethical-legal sources in addition to the revised Common Rule. Physicians acting as investigators and patients serving as research subjects bring to that relationship a long history regarding consent to treatment, and everyone dealing with research ethics needs to be aware of the Nuremberg Code and other human-rights documents. These three streams make separate and distinctly different contributions to informed consent doctrine.

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**Seeing Beyond the Margins:  
Challenges to Informed Inclusion of  
Vulnerable Populations in Research**

*Sarah Gehlert and Jessica Mozersky*

Although the importance of including vulnerable populations in medical research is widely accepted, identifying how to achieve such inclusion remains a challenge. Ensuring that the language of informed consent is comprehensible to this group is no less of a challenge. Although a variety of interventions show promise for increasing the comprehensibility of informed consent and increasing a climate of exchange, consensus is lacking on which interventions should be used in which situations and current regulations provide little guidance. We argue that the notion of individual autonomy — a foundational principle of informed consent — may be too narrow for some vulnerable populations by virtue of its failure to acknowledge their unique histories and current circumstances. It has a different meaning for members of structured groups like American Indians than for unstructured groups, such as African Americans, whose complicated histories foster group identity. Ensuring broad participation in research and selecting appropriate methods for obtaining informed consent — namely, methods aligned with the source of vulnerability and level of risk — require new ways of thinking that might produce guidelines for matching informed consent models and processes with subpopulations.

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**Personal Experiences with Tribal  
IRBs, Hidden Hegemony of  
Researchers, and the Need for an  
Inter-cultural Approach: Views from  
an American Indian Researcher**

*J. Neil Henderson*

In approximately the last 20 years, the self-protection capacity of many American Indian tribes has significantly increased to include the review of research requests by a tribally based IRB. While these tribal IRBs are trained using a curriculum derived from the Belmont Report, there is need to recognize the cultural specificity of the Belmont Report and its potential for conflict or inappropriateness when applied to populations with deep differences in cultural constructs compared to the majority population. However, recognition of the sometimes paradigmatically different culture of American Indian tribes compared to the U.S. culture at large seldom occurs. Moreover, significant and subtle factors of researchers' professional, organizational, and personal cultures that relate to the research enterprise are essentially never addressed by themselves or the tribal IRB. Nonetheless, tribal IRBs continue and serve as a procedural guide for investigators intending to conduct respectful research with American Indian populations.

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**Avoiding Exploitation in Phase I  
Clinical Trials: More than (Un)Just  
Compensation**

*Matt Lamkin and Carl Elliott*

Lowering compensation to research subjects to protect them from "undue inducement" is a misguided attempt to shoehorn a concern about exploitation into the framework of autonomy. We suggest that oversight bodies should be less concerned about undue influence than about exploitation of subjects. Avoiding exploitation in human subjects research requires not only increasing compensation, but enhancing the dignity of research participation.

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**The Ethics of Using Complementary  
Medicine in Pediatric Oncology Trials:  
Reconciling Challenges**

*Amy S. Porter and Eric Kodish*

Medication reconciliation for pediatric oncology patient-participants enrolled in clinical trials often reveals the use of chemical complementary medicine alongside protocol therapeutic agents. Considering the blurry delineation between clinical ethics and research ethics, this paper demonstrates how complementary medicine-related protocol violations introduce ethical questions of who should be included and excluded from clinical trials and offers recommendations on how to manage physician-patient-family interactions around these challenging issues.

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**Capacity, Vulnerability, and Informed  
Consent for Research**

*Michelle Biros*

This article presents an overview for clinician investigators on the concepts of decision-making capacity and vulnerability as related to human subjects research. Tools for capacity assessment and unacknowledged sources of vulnerability are discussed, and the practical gaps in current informed consent requirements related to impaired capacity and potential vulnerability are described. Options are suggested for research discussions when full regulatory consent is not possible and an exception from informed consent does not apply.

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**Informed Consent in Translational  
Genomics: Insufficient Without  
Trustworthy Governance**

*Wylie Burke, Laura M. Beskow, Susan  
Brown Trinidad, Stephanie M. Fullerton,  
and Kathleen Brelsford*

Neither the range of potential results from genomic research that might be returned to participants nor future uses of stored data and biospecimens can be fully predicted at the outset of a study. Informed consent procedures require clear explanations about how and by whom decisions are made and what principles and criteria apply. To ensure trustworthy research governance, there is also a need for empirical studies incorporating public input to evaluate and strengthen these processes.

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**Pragmatic Tools for Sharing Genomic  
Research Results with the Relatives  
of Living and Deceased Research  
Participants**

*Susan M. Wolf, Emily Scholtes, Barbara  
A. Koenig, Gloria M. Petersen, Susan A.  
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Bonnie S. LeRoy, Noralane M. Lindor, P.  
Pearl O'Rourke, Carmen Radecki Breitkopf,  
Mark A. Rothstein, Brian Van Ness, and  
Benjamin S. Wilfond*

Returning genomic research results to family members raises complex questions. Genomic research on life-limiting conditions such as cancer, and research involving storage and reanalysis of data and specimens long into the future, makes these questions pressing. This author group, funded by an NIH grant, published consensus recommendations presenting a framework. This follow-up paper offers concrete guidance and tools for implementation. The group collected and analyzed relevant documents and guidance, including tools from the Clinical Sequencing Exploratory Research (CSER) Consortium. The authors then negotiated a consensus toolkit of processes and documents. That toolkit offers sample consent and notification documents plus decision flow-charts to address return of results to family of living and deceased participants, in adult and pediatric research. Core concerns are eliciting participant preferences on sharing results with family and on choice of a representative to make decisions about sharing after participant death.

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**Design Issues in E-Consent**

*John Wilbanks*

Electronic informed consent represents an opportunity to redesign the way that participants understand and elect to enroll in clinical research studies. However, electronic consent faces certain barriers common to all informed consent processes and other barriers specific to the technical environment. At Sage Bionetworks, we designed an electronic consent process as a software product and released it as an open source tool. We believe that using contemporary design processes to intentionally create cognitive friction, where potential study participants are confronted with interfaces that require them to slow down and contemplate study concepts, offers a significant opportunity for ethical design as research increasingly uses smartphones and digital methodologies.

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**Health Research with Big Data: Time for  
Systemic Oversight**

*Effy Vayena and Alessandro Blasimme*

To address the ethical challenges in big data health research we propose the concept of systemic oversight. This approach is based on six defining features (adaptivity, flexibility, monitoring, responsiveness, reflexivity, and inclusiveness) and aims at creating a common ground across the oversight pipeline of biomedical big data research. Current trends towards enhancing granularity of informed consent and specifying legal provisions to address informational privacy and discrimination concerns in data-driven health research are laudable. However, these solutions alone cannot have the desired impact unless oversight activities by different stakeholders acquire a common substantive orientation.

## Independent Articles

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### **A Genomically Informed Education System? Challenges for Behavioral Genetics**

*Maya Sabatello*

The exponential growth of genetic knowledge and precision medicine research raises hopes for improved prevention, diagnosis, and treatment options for children with behavioral and psychiatric conditions. Although well-intended, this prospect also raises the possibility — and concern — that behavioral, including psychiatric genetic data would be increasingly used — or misused — outside the clinical context, such as educational settings. Indeed, there are ongoing calls to endorse a “personalized education” model that would tailor educational interventions to children’s behavioral and psychiatric genetic makeup. This article explores the justifications for, and prospects and pitfalls of such endeavors. It considers the scientific challenges and highlights the ethical, legal, and social issues that will likely arise should behavioral genetic data become available (or be perceived as such) and are routinely incorporated in student education records. These include: when to disclose students’ behavioral and psychiatric genetic profile; whose genomic privacy is protected and by whom; and how students’ genetic data may affect education-related decisions. I argue that the introduction of behavioral genetics in schools may overshadow the need to address underlying structural and environmental factors that increase the risk for psychiatric conditions of all students, and that the unregulated use of student behavioral genetic profiles may lead to unintended consequences that are detrimental for individuals, families and communities. Relevant stakeholders — from parents and students to health professionals, educators, and policy-makers — ought to consider these issues before we forge ahead with a genomically informed education system.

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### **Opening Closed Doors: Promoting IRB Transparency**

*Holly Fernandez Lynch*

Institutional Review Boards (IRBs) have substantial power and authority over research with human subjects, and in turn, their decisions have substantial implications for those subjects, investigators, and the public at large. However, there is little transparency about IRB processes and decisions. This article provides the first comprehensive taxonomy of what transparency means (or could mean) for IRBs — answering the questions “to whom, about what, and by what mechanisms?” It also explains why the status quo of nontransparency is problematic, and presents arguments for greater transparency from the perspective of a variety of stakeholders. IRB transparency will make boards more accountable, improve the quality of their decision-making, facilitate consistency in board decisions, permit empirical study of IRBs, promote research efficiency, and advance trust in the research enterprise, among a variety of other benefits. Regulators should promote IRB transparency, IRBs themselves should commit to sharing as much information as they can within the confines of confidentiality requirements, and investigators can endeavor to take matters into their own hands by sharing IRB correspondence and IRB-approved protocols and consent materials.

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### **Child Trafficking: Issues for Policy and Practice**

*V. Jordan Greenbaum, Katherine Yun, and Jonathan Todres*

Efforts to address child trafficking require intensive collaboration among professionals of varied disciplines. Healthcare professionals have a major role in this multidisciplinary approach. Training is essential for all professionals, and policies and protocols may assist in fostering an effective, comprehensive response to victimization.

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### **Reducing Regulatory Burdens on Research with Human Subjects: A Case Study of the Transition to the Final Common Rule at Boston Medical Center and Boston University Medical Campus**

*Fanny K. Ennever*

Boston Medical Center/Boston University Medical Campus recently reduced certain requirements for human subjects research where this could be done without adversely affecting the rights and welfare of participants, in anticipation of changes in the Final Common Rule. Modifications affected exempt and expedited categories, approval periods, ceding review, Quality Improvement/Quality Assessment activities, and some requirements for pregnant women, prisoners, and children. This case study may assist other institutions in responding to the Final Common Rule.

**Symposium articles** are solicited by the guest editor for the purposes of creating a comprehensive and definitive collection of articles on a topic relevant to the study of law, medicine and ethics. Each article is peer reviewed.

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**Opioid, Law & Ethics**

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by Abbe R.  
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